International Journal of Cardiology and Cardiovascular Medicine

ISSN 2517-570X

Functional Cardiac Parameters Calculated in Early Diabetes using 64 Slice CT Scanner

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Abstract

Aims: The study aimed at evaluation of the feasibility of cardiac MDCT for assessment of diastolic function in asymptomatic diabetic patients as compared to echocardiography and to study the intermodality correlation of observed findings.

Methods: A total of 15 normotensive, non-coronary artery disease (CAD) diabetic patients and 15 age-matched asymptomatic controls were included in the study. All of them underwent 2D echocardiography with Tissue Doppler Imaging and MDCT. LV volume and LV length were calculated and were plotted against time. Further, early (E) and late (A) transmitral peak velocities (cm/s) and peak mitral septal tissue velocity (Ea; cm/s) were derived for the assessment of diastolic dysfunction and LV filling pressure (E/Ea) was also estimated.

Results: A total of 73.3% (11 out of 15) patients showed diastolic dysfunction by both MDCT and echocardiography. Good correlation was observed between cardiac MDCT and 2D echocardiography for assessment of E ($r=0.992$; $p<0.001$), A ($r=0.974$, $p<0.001$), E/A ($r=0.979$; $p<0.01$), Ea ($r=0.977$; $p<0.001$), and E/Ea ($r=0.994$; $p<0.001$).

Conclusions: Our study showed good correlation between MDCT and echocardiography for assessment of diastolic dysfunction in asymptomatic normotensive diabetic patients. Hence, cardiac MDCT can be used a problem solving tool along with echocardiography for assessing LV diastolic function. It does not replace echocardiography but rather extends its capabilities and offers advantages in various clinical settings.

Keywords

LV diastolic dysfunction; Cardiac multidetector row CT; Tissue doppler imaging

Introduction

Diabetes mellitus is one of the most common chronic diseases affecting millions of people worldwide. Several large epidemiological studies have consistently reported diabetes as a strong risk factor for the development of cardiovascular diseases. Diabetes inflicts a direct insult to the myocardium, with cellular, structural and functional changes manifest as the diabetic myocardial phenotype. Diastolic heart failure was traditionally considered a comparatively rare and benign disorder when compared to systolic heart failure. Large observational studies have recently shown that diastolic heart failure accounts for approximately 50% of all heart failure cases [1], and its prevalence is growing [2]. Up to 37% of individuals with diastolic heart failure have diabetes [3]. Diabetic cardiomyopathy is defined as ventricular dysfunction occurring independently of coronary artery disease (CAD) and hypertension. Echocardiography and Doppler imaging have been the traditional and most commonly performed non-invasive investigations for left ventricular function assessment [4-6]. Despite the impressive impact of isolated diastolic dysfunction upon mortality, there remains a lack of evidence-based treatment regimens for diastolic dysfunction. Also, the data pertaining to the prevalence of diastolic dysfunction in asymptomatic diabetic subjects are scanty as it is not always detected early. Whereas an electrocardiogram and chest X-ray are obtained routinely but are only occasionally helpful for detecting left ventricular hypertrophy or dilatation. Therefore, more sensitive imaging techniques are required for the early detection of myocardial dysfunction. Recently Cardiac multidetector computed tomography (MDCT) has emerged as a potent non-invasive imaging modality for the evaluation of coronary atherosclerosis [7]. So far, multiphase CT studies have been mostly restricted to cardiac morphology and LV systolic function analysis [8] and very little information is available on the feasibility of cardiac MDCT imaging to assess diastolic LV function. The information that is needed for evaluation of diastolic function can be derived from multiphase CT without additional image acquisition or radiation dose.

Article Information

DOI: 10.31021/ijccm.20181113
Article Type: Research Article
Journal Type: Open Access
Volume: 1 **Issue:** 3
Manuscript ID: IJCCM-1-113
Publisher: Boffin Access Limited

Received Date: 11 July 2018
Accepted Date: 09 August 2018
Published Date: 15 August 2018

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Citation: Dwivedi AND, Agarwal A, Agarwal V, Tripathi S, Tripathi K. Functional cardiac parameters calculated in early diabetes using 64 Slice CT Scanner. Int J Cardiol Cardiovasc Med. 2018 Aug;1(3):113

MDCT has the potential to meet the present need for a robust tool that can establish diagnostic efficacy in future studies. The present study aimed to assess LV diastolic function in asymptomatic diabetic population before appearance of clinical symptoms using cardiac MDCT and echocardiography and their intermodality agreement as a prognostic tool of cardiac mortality in diabetic patients.

Methods

The present study was a "prospective analytical case control study" performed after obtaining due approval from the institutional review board. The study was conducted from July 2014 to August 2015. Asymptomatic normotensive non CAD diabetic patients were compared to age matched asymptomatic normotensive non CAD non-diabetic individuals for evaluation of diastolic dysfunction by echocardiography and MDCT. Diagnosis of diabetes mellitus was made according to the National Diabetes Data Group and WHO diagnostic criteria [9,10]. Diastolic dysfunction by echocardiography was defined according to ASE/EACVI guidelines [11]. A total of 30 subjects were recruited for the study (15 asymptomatic diabetic patients and 15 healthy controls without diabetes). Written informed consent was obtained from all the participants prior to their enrolment in this study for undergoing 2D echocardiography and MDCT. All the participants were informed about the protocol. Cases were included in the study protocol if they met the following criteria: (i) Diabetic patients, (ii) age range of 25-60 years, (iii) asymptomatic patients without diabetic complications, hypertension, hyperlipidemia or features of coronary artery disease (CAD). Exclusion criteria set for the study were: (i) Hypertension, (ii) Dyslipidaemia, (iii) Obesity, (iv) Females planning pregnancy, (v) Valvular heart disease, (vi) Congestive heart failure, (vii) history of CAD. The purpose was to exclude other parameters which can cause diastolic dysfunction independent of diabetes as hyperlipidemic, advanced age, hypertension and valvular heart disease and may act as confounding factors. Age-sex-BMI- matched healthy non-diabetic & normotensive individuals were selected as the controls, whose blood tests, 2-D echo and MDCT were done with their consent for comparison with the cases.

Echocardiography

All the subjects underwent 2D echocardiography first; LV diastolic function assessment being done by conventional Doppler along with the Valsalva maneuver, Tissue Doppler imaging (TDI), and color M-mode flow propagation velocity. The Modified Simpson's or Bullet method techniques were used for the calculation of LV ejection fraction and LV mass was determined by the area-length method. The following velocities and times were recorded with conventional Doppler at the mitral inflow as well as at the entrance of the pulmonary veins into the left atrium: Early ventricular filling (E), flow related to atrial contraction (A), Deceleration Time (DT), Isovolumic Relaxation Time (IVRT) and E/A ratio. Measurements were averaged from 3 end-expiratory cycles. Subjects were also made to perform Valsalva maneuver while echocardiography. Mitral inflow measurements (E and A) were obtained during phase II (straining) of the Valsalva maneuver. The maneuver was considered valid only if there was a 10% decrease in E velocity compared with baseline. Diastolic dysfunction was considered to be present in the current study if the change in the E/A ratio was ≥40% from baseline after the Valsalva maneuver.

Early diastolic mitral annular velocity was assessed by using pulsed wave TDI of both the septal and lateral walls in the apical 4-chamber view (averaged from 3 cardiac cycles). Both septal and lateral walls ≥8 cm/s demonstrated Diastolic LV dysfunction in our study. Diastolic dysfunction was considered to be present if diastolic abnormality was found with any of the echocardiographic approaches *viz.* conventional Doppler, the effects of the Valsalva maneuver on transmitral flow velocities and TDI.

Next, MDCT imaging was performed with a 64-slice helical scanner. Before the scan, patients were monitored for blood pressure and heart rate. Patients with heart rate >65 beats/min were given metoprolol 50 to 100 mg orally, unless contraindicated. We did not use nitroglycerin. The renal function test of all the subjects was done as we had to use contrast for MDCT. Scan parameters used were-Scan type Cardiac helical, Pitch 0.160:1, Table speed row 6.4, Rotation time 0.35 sec, Slice thickness 0.625, Beam collimation 40 mm, Voltage 120 kVp, Current 500 mA, Recon type Standard SSB, Scan length 10 cm. CT Post processing was performed with advantage work station. Multisegment reconstruction algorithms were used for analysis. By retrospective ECG-gating our MDCT divided each cardiac cycle into 10 phases and LV volume and LV length were calculated for each phase. This LV volume was plotted against time. Then, we calculated the difference in LV volume for each consecutive phase per second, which was again plotted against time. This graph gave the values of Early (E) and Late (A) peak transmitral velocities (Figure 1). These values were divided with respective transmitral area in E phase and A phase which gave us the values of E and A comparable to 2-D Echo (Figure 2). By the ratio of E and A (E/A) we can calculate the diastolic dysfunction. Likewise, we plotted a graph of LV length v/s time. We then plotted change in LV length per second v/s time. This graph gave us the value of Ea (peak mitral septal tissue velocity in early diastole). By calculating E/Ea (LV filling pressures) we can estimate diastolic dysfunction (Figure 3).

Transmitral Velocity=Transmitral flow (mL/s)/Mitral Valve Area (mm^2)

Diastolic function was graded in 4 categories [11] using the following criteria:

1. Normal diastolic function (≥ 1 E/A<2 and E/Ea ≤ 8);
2. Impaired relaxation pattern (diastolic dysfunction grade I; E/A<1 and E/Ea ≤ 8);
3. Pseudo normal pattern (diastolic dysfunction grade II; ≥ 1 E/A<2 and ≥ 9 E/Ea ≤ 12); and
4. Restrictive filling pattern (diastolic dysfunction grade III; E/A ≥ 2 and E/Ea ≥ 13).

E is peak transmitral velocity in early diastole where A is peak transmitral velocity in late diastole. The ratio E/A, gives a measure of diastolic dysfunction. When E is divided by variable Ea, mitral septal tissue velocity in early diastole (E/Ea) we get LV filling pressure.

Statistical analysis

The intergroup and intermodality comparisons of variables obtained was done by applying *t*-test and chi-square test by using the SPSS software (SPSS version 17.0; SPSS, Chicago, IL, USA). A p-value<0.05 was considered to be statistically significant for various results in the study.

Results

A total of 15 normotensive diabetic patients were included in the study as cases. The mean age was 48.20 ± 9.283 years. Table 1 shows the baseline characteristics of the study population for both Diabetics and non-diabetics. None of the values show significant difference except for fasting blood sugar and HbA1c depicting that our cases and controls were comparable for all characteristics except for Diabetes. Above table also signifies that our study population is normotensive and none of them are obese or hyperlipidemic. Thus, we successfully excluded any confounding factor which may contribute to diastolic dysfunction by itself.

On statistical analysis we found that there is a significant difference between diabetic subjects and non-diabetic normal population in the values of E (p=0.039), E/A ratio (p=0.017) and Ea (p=0.000) as measured in on 2-D Echocardiography and E (p=0.036), E/A ratio (p=0.033) and Ea (p=0.000) as measured on MDCT (Table 2). Hence, it can be said that these parameters were comparable between 2D echocardiography and MDCT for the study groups.

In our study, total 73.3% people were observed to have grade I to grade II diastolic dysfunction on echocardiography and MDCT. None of them had grade III (Restrictive filling pattern) diastolic dysfunction (Table 3).

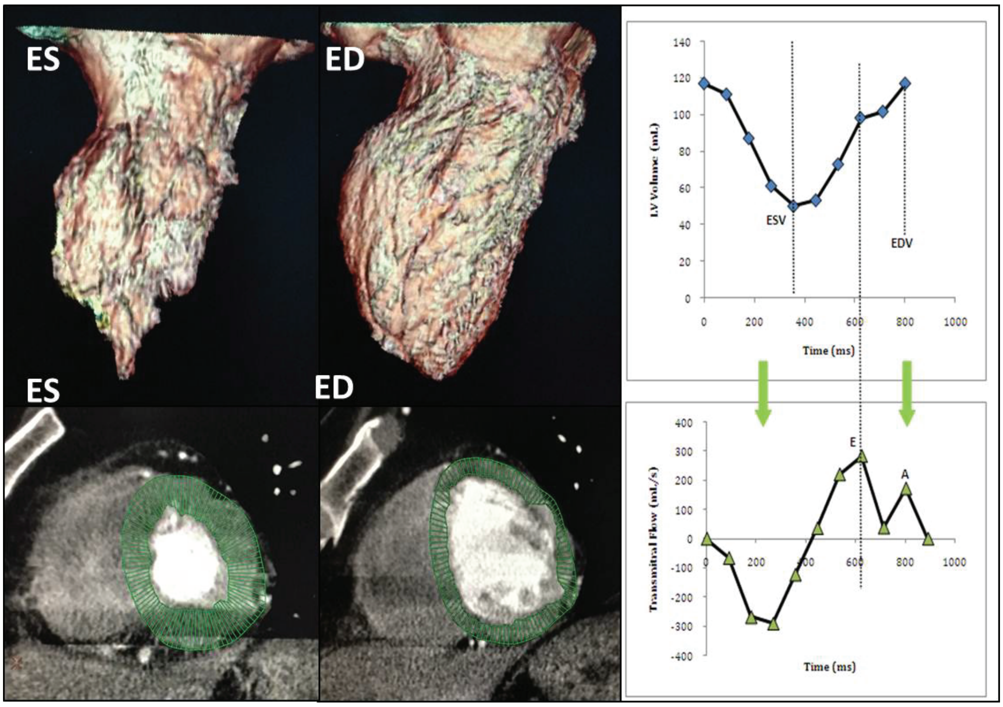

Figure 1: Transmitral flow: left ventricular (LV) volumes were measured for 10 phases per cardiac cycle, using short-axis images by outlining endocardial contours in each phase. They were then plotted in a volume versus time curve (right upper). Changes in LV volumes between 2 consecutive phases were plotted against time (transmitral flow vs. time curve) (right lower). Subsequently, early and late peak transmitral flows (ml/s) were derived

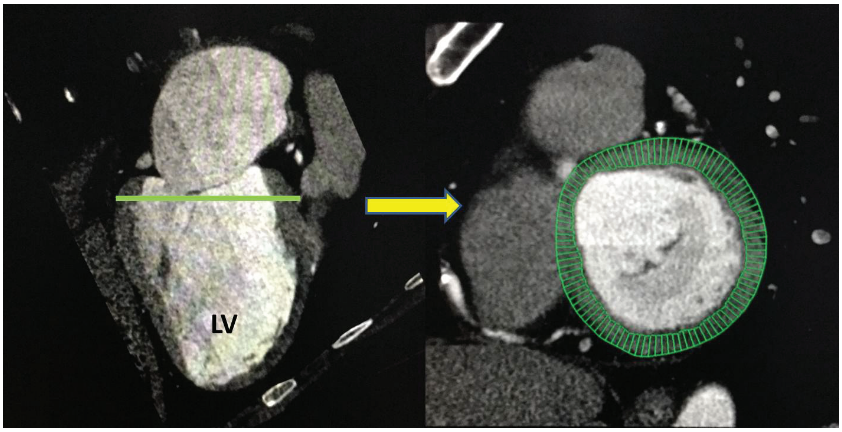

Figure 2: Mitral valve area: Measurements were taken at the most distal level of the mitral valve leaflets (smallest mitral valve area) using reconstructed images at peak early and late transmitral velocities. The mitral valve area was measured at the tip of the leaflets on short-axis views

Diastolic dysfunction E/Ea ratio is similar as in normal diastolic function (asymptomatic) diabetic patients. Most of our subjects have Grade I diastolic dysfunction. Further, correlation was done between diastolic parameters of 2D Echocardiography and MDCT in both the study groups. All the diastolic parameters had good correlation between echocardiography and MDCT in the study population (Table 2).

In diabetics, we observed good correlation in 2D echocardiography and MDCT between peak transmitral velocity in early diastole (E) (Correlation coefficient r=0.992, p-value<0.001), peak transmitral velocity in atrial systole (A) (r=0.974, p-value<0.001), E/A (r=0.979, p-value<0.001), early peak transmitral septal velocity (r=0.977, p-value<0.001) and E/Ea (r=0.994, p-value<0.001), which was statistically proven to make the findings on 2D echocardiography and MDCT comparable. The p value is calculated for various diastolic parameters in diabetic subpopulation and correlation coefficient, r is calculated.

Discussion

Diastolic myocardial dysfunction with a normal left ventricular ejection fraction is clinically important because it accounts for approximately 50% of all hospital admissions for acute heart failure [12]. The delay in diagnosis is due to patient-related factors and partly to medical oversight [13]. The traditional echocardiographic and Doppler techniques have proved inconclusive for the diagnosis of diastolic dysfunction in diabetic cardiomyopathy and in the metabolic syndrome because there is no consensus regarding definitive diagnostic criteria [14]. Present study aimed at early diagnosis of diastolic dysfunction in asymptomatic diabetic subjects by Multidetector row CT (MDCT) and comparison of MDCT findings

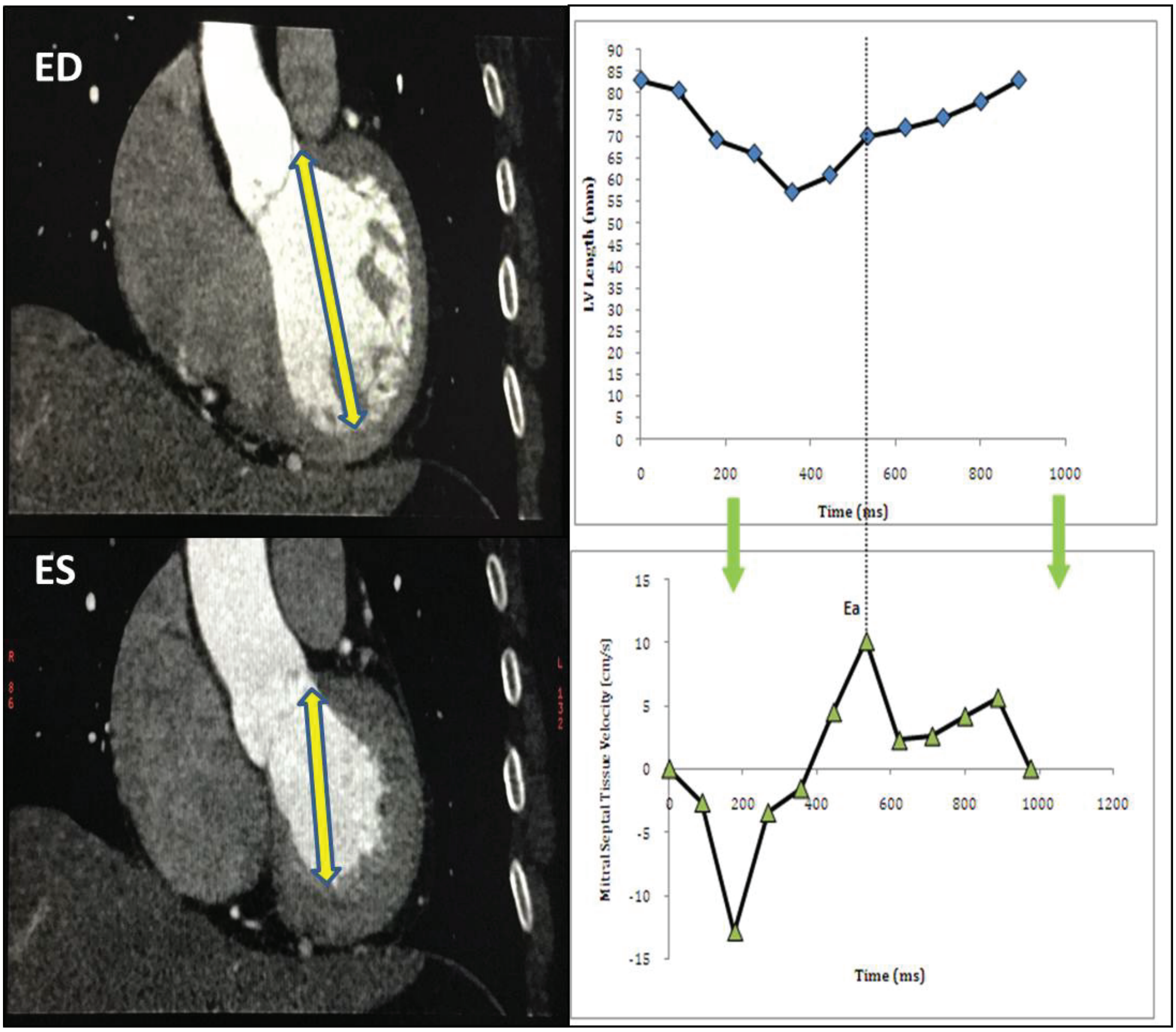

Figure 3: Mitral septal tissue velocity: anatomic markers were positioned at the mitral septal annulus and cardiac apex. The LV length (cm) was calculated for each phase and plotted in a LV length versus time curve (right upper). Next, changes in LV length between 2 consecutive phases were calculated. Based on these numbers, mitral septal tissue velocities (cm/s) were calculated for each phase (velocity vs. time curve) (right lower)

Characteristics	Diabetics (Mean ± SD)	Non-diabetics (Mean ± SD)	p-value
Age (yr)	48.20 ± 9.283	50.87 ± 5.630	.350
Pulse Rate (/min)	71.33 ± 5.473	68.27 ± 4.935	.118
SBP (mm Hg)	116.53 ± 11.963	116.67 ± 8.837	.973
DBP (mm Hg)	70.53 ± 5.041	67.87 ± 4.307	.131
BMI (kg/$m^{2)}$	21.1200 ± 1.06382	20.9867 ± .86344	.709
HBA_{1c} (%)	9.5373 ± 1.98740	5.1400 ± .43556	.0001
FBS (mg/dL)	124.733 ± 38.5421	92.333 ± 9.4855	.004
Chol (mg/dL)	39.27 ± 31.183	41.40 ± 28.830	.016
TGA (mg/dL)	120.13 ± 28.468	122.40 ± 13.076	.781
HDL (mg/dL)	57.00 ± 10.981	60.80 ± 10.101	.332
LDL (mg/dL)	71.67 ± 29.796	56.33 ± 10.761	.071
VLDL (mg/dL)	22.1600 ± 6.63204	20.5000 ± 3.54482	.04

Table 1: Baseline Characteristics of the Cases (diabetics) and Controls (non-diabetics)

Diastolic parameters	2-D Echocardiography				MDCT			
	Diabetics Mean ± SD	Non-diabetics Mean ± SD	t- value	p-value	Diabetics (Mean ± SD)	Non-diabetics (Mean ± SD)	t- value	p-value
E (cm/s)	71.11 ± 19.18	84.00 ± 12.73	-2.169	0.039	68.47 ± 18.85	81.28 ± 12.36	-2.200	0.036
A(cm/s)	76.11 ± 20.08	66.59 ± 12.52	1.557	0.131	75.58 ± 20.99	66.28 ± 16.26	1.356	0.185
E/A	1.00 ± .36	1.28 ± .23	-2.548	0.017	1.02 ± .41	1.18 ± .28	-2.090	0.033
Ea (cm/s)	9.95 ± 2.09	13.01 ± 1.51	-4.582	0.000	9.83 ± 2.14	12.77 ± 1.45	-4.383	0.000
E/Ea	7.25 ± 1.73	7.22 ± 1.72	0.047	0.962	7.08 ± 1.72	6.38 ± .67	1.453	0.157

Table 2: Diastolic Function Parameters for 2-D Echocardiography and MDCT in diabetic patients and non-diabetics (controls)

Diastolic Dysfunction (DD) Grade	Echocardiography (n=15) No. (%)	MDCT (n=15) No. (%)
Normal	4 (26.7)	4 (26.7)
Grade 1 DD	10 (66.67)	10 (66.67)
Grade 2 DD	1 (6.67)	1 (6.67)
DD	11 (73.3)	11 (73.3)
Total	15 (100)	15 (100)

Table 3: Diastolic Dysfunction (DD) in cases as detected by 2D Echocardiography and MDCT

with 2D echocardiography findings. It also aimed to compare the prevalence of diastolic dysfunction in diabetic population and healthy, non-diabetic but otherwise matched controls and see whether the difference is statistically significant. In our study, both in 2D echocardiography and MDCT, 73.3% diabetic patients showed diastolic dysfunction (DD) as compared to only 13.3% of non-diabetics. The difference between the two groups was statistically significant (p=0.001). Additionally, among diabetics ten patients having diastolic dysfunction had Grade 1 DD whereas only one patient had Grade 2 DD. In non-diabetics (controls), 2 subjects had Grade 1 diastolic dysfunction. Significantly high prevalence of LV diastolic dysfunction in normotensive patients with type 2 diabetes mellitus without coronary heart disease was observed in our study. Zabalgoitia et al. [15] also found 30% prevalence of diastolic dysfunction in similar group of patients using conventional Doppler study. This might be an underestimation, because diagnosing diastolic dysfunction by conventional Doppler is limited in the setting of elevated LV end-diastolic pressure and an apparently normal transmitral flow velocity spectral Doppler pattern. This same group of investigators obtained comparable results to other investigators [16] with the use of the Valsalva maneuver to unmask diastolic dysfunction in a significant proportion of these patients. Thus, to determine occult diastolic dysfunction at an earlier preclinical stage in normotensive diabetics, cardiac ultrasound imaging needs to be extended by using TDI and Valsalva maneuver. Boyer et al. [17] in their study found diastolic dysfunction in 75% of patients when these echocardiographic techniques were used. In diabetics, we observed good correlation in 2D echocardiography and MDCT between peak transmitral velocity in early diastole (E) (Correlation coefficient r=0.992, p-value<0.001), peak transmitral velocity in atrial systole (A) (r=0.974, p-value<0.001), E/A (r=0.979, p-value<0.001), early peak transmitral septal velocity (r=0.977, p-value<0.001) and E/Ea (r=0.994, p-value<0.001), which was statistically proven to make the findings on 2D echocardiography and MDCT comparable. This is in line with the study of Boogers et al. [18] where in 70 patients showed good correlations for same diastolic parameters on Cardiac CT as compared to 2D echocardiography in patients with known or established CAD.

Conlusions

Thus our study showed that normotensive, asymptomatic patients with diabetes and normal LV systolic function may exhibit diastolic dysfunction. Accordingly, additional post processing for diastolic dysfunction may have the potential to enhance the clinical evaluation derived from cardiac CT. There is a high prevalence of LV diastolic dysfunction with preserved systolic function in asymptomatic diabetic patients. MDCT should be used to identify (pre-) diabetic individuals with diastolic dysfunction and to optimize their clinical management.

Conflicts of Interest

There is no financial/personal interest to declare.

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